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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,239	12/08/2000	James Blake	02558P-001340US	1694

20350 7590 05/31/2006

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EXAMINER
LE, EMILY M

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/733,239	BLAKE ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,48 and 49* is/are pending in the application.

4a) Of the above claim(s) *14-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 48-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03/22/2006 has been entered.

Status of Claims

2. Claims 29-47 are cancelled. Claims 48-49 are added. Claims 1-28 and 48-49 are pending. Claims 14-28 are withdrawn from consideration as being directed to a non-elected invention. Claims 1-13 and 48-49 are under examination.

Specification

3. The disclosure is objected to because of the following informalities: It is noted that this application appears to claim subject matter disclosed in prior Application No. 08/462749, 08/1400696, 07/532429, and 07/360513. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. See MPEP § 201.11.

4. Additionally, the use of the trademarks, such as Tween 20 ™, cited at line 33 on page 25, and Sephadex ™, cited at line 25 on page 20, have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 49 is a newly added claim. The claim requires the solid phase be a latex bead entrapped on a microporous membrane. To provide support for the newly added claim, Applicant cited lines 32-36 on page 16, and line 34 on page 27 to line 7 on page 28. In the instant, the Office has reviewed the entire specification, including the passages cited by Applicant; however, support (express, implicit or inherent) for the cited limitation, latex bead entrapped on a microporous membrane cannot be found.

Meanwhile, the Office does note adequate written description for a latex bead, and microporous membrane containing latex beads with a peptide immobilized onto the beads, wherein the peptide immobilized latex beads are entrapped in a microporous membrane. Appropriate correction is required.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-3, 7-9 and 48-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cosand et al., [1] in view of Rosen et al.[2] and Storey et al.[3]

The claims are directed to a composition comprising an isolated peptide, wherein the peptide is immobilized on a solid phase support following the synthesis and cleavage of the peptide from a synthesis solid support, comprises at least one epitope that is capable of binding to antibodies; and comprises an amino acid sequence of 6 to 50 amino acids, wherein the sequence comprises two Cys residues that are separated from one another by at least 2 but fewer than 20 non-Cys amino acid residues, and wherein the thiol groups of the Cys residues are reversibly protected from oxidation by a

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[1] Cosand et al. U.S. Patent No. 4629783, published December 16, 1986.
[2] Rosen et al. WO 87/06005, published October 08, 1987.
[3] Storey et al. Studies on polypeptides. LI. Application of S-ethylcarabmoylcysteine to the synthesis of a protected heptatetracontapeptide related to the primary sequence of ribonuclease T_1. Journal of the American Chemical Society, August 23, 1972, Vol. 94, No. 17, 6170-6178.

chemically reversible means that is resistant to the highly acidic condition used during cleavage of the peptide from its synthesis solid support.

Claim 2, which depends on claim 1, requires the thiol groups be protected from oxidation by ethylcarbamoyl, acetamidolmethyl; 3-nitro-2-pyridinesulfinyl or diphenyl-4-pyridylmethyl. Claim 3, which depends on claim 2, requires the thiol groups be protected from oxidation by ethylcarbamoyl. Claim 7, which depends on claim 1, requires the Cys residues be separated by one another by 4 to 6 non-Cys residues.

Claim 8, which depends on claim 1, requires the peptide to be capable of binding to antibodies to a retroviral transmembrane protein. Claim 9, which depends on claim 8, defines the retroviral protein as an HIV-1 gp41, and requires the peptide to comprise at least seven contiguous amino acids within SEQ ID NO: 1.

Claim 48, which depends on claim 1, requires the highly acidic cleavage condition to comprise hydrofluoric acid (HF) or trifluoroacetic acid (TFA). Lastly, claim 49, which depends on claim 1, requires the solid phase to be a microtiter, a glass bead, a latex bead entrapped on a microporous membrane, a tube, a filter or a chromatographic surface.

Cosand teaches several peptides that are capable of binding to antibodies. One of the peptide that Cosand teaches is a peptide V. Peptide V has the following sequence: Arg-Ile-Leu-Ala-Val-Glu-Arg-Tyr-Leu-Lys-Asp-Gln-Gln-Leu-Leu-Gly-Ile-Trp-Gly-Cys-Ser-Gly-Lys-Leu-Ile-Cys. [Lines 30-40, column 5.] Peptide V has 26 amino acid residues in length. Thus, Peptide V does comprise an amino acid sequence of 6 to 50 amino acids. Peptide V comprises two Cys residues that are separated from one

another by 5 non-Cys residues. Thus, Peptide V comprises two Cys residues that are separated from one another by at least 2 but fewer than 20 non-Cys amino acid residues, and Cys residues that are separated by one another by 4 to 6 non-Cys residues. Peptide V is amidated at the C-terminus. Additionally, peptide V is 100% identical to the amino acid sequence set forth in SEQ ID NO: 1. Peptide V comprises the 26 amino acid residues that correspond to a part of the HIV gp41 protein.

Cosand also teaches immobilizing the peptides to the solid phase support following the synthesis of the peptide from a synthesis solid support. The solid phase support used by Cosand includes chromatographic surfaces and microtiter plates. [Column 10, and Tables 1-3.]

The difference between the claimed invention is: The thiol group present in the peptide of Cosand is not reversibly protected from oxidation by a chemically reversible means, including ethylcarbamoyl, that is resistant to the highly acidic condition used during cleavage of the peptide from its synthesis solid support. It should be noted that the highly acidic condition used by Cosand during cleavage of the peptides comprises hydrofluoric acid (HF). [Lines 7-15 of column 10.]

However, Rosen et al. teaches that peptides that possess more than two cysteine residues may form cyclic monomers, linear or cyclic dimers, and linear polymers of various lengths due to the reduction of the thiol group present on cysteine residues by oxidation. [Lines 15-30 of page 10] Rosen et al. further notes that the cyclic monomer of the peptides is believed to be less efficient in binding to the microtiter wells, and is less suited as a solid phase component of the Enzyme-Linked Immunosorbent

Assay (ELISA), which Rosen et al. used to detect for the presence of HIV related antibodies. [Lines 27-35 of page 22]

And Storey et al. teaches the use of ethylcarbamoyl to reversibly protect cysteine residues from oxidation. Specifically, Storey et al. uses ethylcarbamoyl to protect cysteine from the highly acidic highly acidic condition used during cleavage of the peptide from its synthesis solid support. Storey et al. notes that ethylcarbamoyl is stable toward strong acid. [Sulfhydryl Protection section, page 6171.] Hence, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to use ethylcarbamoyl to reversibly protect cysteine from oxidation. One of ordinary skill in the art at the time the invention was made would have been motivated to do so to control the oxidative form of peptides comprising more than one cysteine residue, and to provide a suitable solid phase component of the Enzyme-Linked Immunosorbent Assay (ELISA). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because the use of ethylcarbamoyl to protect cysteine from the highly acidic condition used during cleavage of the peptide from its synthesis solid support is routinely practiced in the art.

9. Claims 1, 4-6, 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cosand et al., in view of Rosen et al. and Storey et al., as applied to claims 1 and 8-9, in further view of Cosand et al.[4]

Claim 4, which depends on claim 1, requires the peptide to comprise a third Cys residue at the N-terminus of the peptide, wherein the third Cys residue is not protected

from oxidation. Claim 5, which depends on claim 4, specifies that the sequence Cys-Gly-Gly be at the N-terminus of the peptide. Claim 6, which depends on claim 4, requires the C-terminus of the peptide be amidated.

Claim 10, which depends on claim 9, requires the N-terminus of the peptide to comprise additional amino acids to enhance specific binding of the antibodies to the protein, and wherein at least one of the additionally amino acids is a third Cys residue, wherein the third Cys residue is not protected from oxidation. Claim 11, which further limits claim 10, requires the third Cys residue be the N-terminal residue of the peptide. Claim 12, which depends on claim 11, specifies that the sequence Cys-Gly-Gly be at the N-terminus of the peptide. Lastly, claim 13, which depends on claim 11, requires the C-terminus of the peptide be amidated.

The significance of Cosand et al., Rosen et al. and Storey et al., as it pertains to claims 1 and 8-9 is provided above. As summarized above, Cosand teaches a peptide is amidated at the C-terminus.

The difference between the claimed invention and the teachings of Cosand et al., Rosen et al. and Storey et al. is: the peptide of Cosand is not modified at the N-terminus with a third cytosine or the sequence Cys-Gly-Gly. However, Cosand does suggest modifying the peptide with the addition of other amino acids including cytosine at the C or N-terminus of the peptide to provide a useful functionality for linking the peptide to a support or other peptides. [Lines 60-68 of column 3 to lines 1-2 of column 4] Furthermore, in U.S. Patent No. 5075211 Cosand et al. teaches the use of cysteine in combination of other intervening amino acid spacers. [Paragraph bridging columns 3-

[4] Cosand et al. U.S. Patent No. 5075211, filed November 14, 1986.

4.] Additionally, in U.S. Patent No. 5075211 Cosand et al. encourages the use of one to three glycine residues as preferred amino acid spacer to facilitate coupling between the peptide and a support or other peptides. Thus, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to add a third cysteine and one to three glycine residues to the N-terminus of a peptide. One of ordinary skill in the art at the time the invention was made would have been motivated to facilitate the coupling of the peptide to a support or other peptides. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for doing so because modification of peptide with amino acid linkers is well practiced in the art.

Conclusion

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Emily Le 5/22/06
Emily Le
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Art Unit 1648